NHGRI-funded Consortia Working Groups Examining Issues of Genomic Medicine and Return of Results

	CSER	Return of Results Consortium	eMERGE	Genomic Medicine Working Group	PAGE
	Program Contact: Lindsey Lund	Program Contact: Chenge Mahomva	Program Contact: Ian Marpuri	Program Contact: Ian Marpuri	Program Conact: Heather Junkins
Informed Consent	***Informed Consent & Governance (convened under both CSER + RoR)***		***Consent, Education, Regulation, & Consultation***		
	Chairs: Paul Appelbaum and Malia Fullerton		Chairs: Andy Faucett and Maureen Smith		
	Mission: Discuss emerging issues and develop new and creative approaches related to informed consent in the context of clinical sequencing; compare and, to the extent feasible, develop standardized consent language and protocols.		Mission: Share and compare methods for returning results, obtaining consent when needed to return research results. Collaborate on models of recruitment of participants based on genotype. Create resource of CLIA/CAP regulations. Establish liaisons with other new and ongoing projects (ROR, CTSA). Explore the intersection between clinical and personal utility on returning result decisions.		
	NHGRI Staff: Joy Boyer		NHGRI Staff: Rongling Li and Nicole Lockhart		
Actionable Variants	***Actionable Variants & RoR***	***Actionability and Implications for RoR***	***Return of Results (formerly Actionable Variants)***		
	Chairs: Jonathan Berg and Gail Jarvik	Chairs: Robert Green and Richard Sharp	Chairs: Gail Jarvik and Iftikhar Kullo		
	Mission: Coordinate approaches to defining and binning genetic variants potentially useful for clinical purposes; share and review external resources for similar purposes. Discuss emerging issues and develop standards related to returning results to study participants (including incidental findings, where determined to be appropriate).	Mission: Analyze the relevant normative and clinical issues, including such issues as whether or when there exists an ethical duty to return results, what are the appropriate normative and clinical criteria for determining whether results should be returned, the meaning of "actionability" and whether "actionability," should be the relevant standard for determining which results are returnable, the relevance of the distinction between research and clinical care and practical issues in the contexts of both research and clinical care.	Mission: Define an initial set of variants that are potentially useful in clinical practice for purposes such as assessment of genetic risk for complex disorders or selection or dosing of drugs. This initial set will focus on common disease risk variants and pgx variants for which we expect to have data. We will assess the levels of evidence supporting these variants and consider the cost and benefit of incorporating them into patient care.		
	NHGRI Staff: Jean McEwen, Sheri Schully (NCI), and Lucia Hindorff	NHGRI Staff: Jean McEwen	NHGRI Staff: Rongling Li		
Sequencing/Genomics	***Sequencing Standards***		***Genomics***	***Sequencing***	
	Chairs: Levi Garraway and Pete White		Chairs: Dana Crawford and David Crosslin	Chairs: Howard Jacob and Scott Weiss	
	Mission: Develop and share technical standards for sequencing in a clinical context (for example, minimum coverage and quality metrics, turnaround time, data formats, CLIA); develop best practices for variant validation.		Mission: A major priority will be imputation of GWAS data across the network to the latest release of 1000 Genomes Project Data. In addition the group will focus on analysis of GWAS datasets for discovery. Lower priorities of the Genomics Workgroup include copy number variant (CNV) analysis and characterization of genetic risk.	Mission: Change the practice of medicine to a point where a whole genome sequence can be routinely ordered for a patient and to use it to improve their healthcare. What is a reasonable set of data that can be used to accurately interpret and use for patient care? Need to develop enough data to convince people that this needs to be in the clinic.	
	NHGRI Staff: Brad Ozenberger		NHGRI Staff: Rongling Li	NHGRI Staff: Teri Manolio	
Phenotype Measures	***Analysis and Phenotype Measures***		***Phenotyping***		***Phenotype Harmonization***
	Chair: Ian Krantz		Chairs: Josh Denny and Peggy Peissig		Chairs: Multiple (see below)
	Mission: Inventory and harmonize outcomes where useful, to maximize cross-study sample sizes; share and review approaches to genotype-phenotype analysis.		Mission: Coordinate and complete network phenotypes, and support covariates for analysis. Create efficient, effective, and transportable phenotyping methods, structure, and standards. Coordinate with all eMERGE workgroups and other networks.		Mission: Harmonize phenotypes to facilitate cross-study PAGE analyses in specific domains: Cancer (Loic Le Marchand) CVD (Nora Franceschini) Diabetes/obesity (Kari North) Exposures (Rebecca Jackson)
	NHGRI Staff: Lucia Hindorff		NHGRI Staff: Rongling Li		NHGRI Staff: Lucia Hindorff
Electronic Reports	***Electronic Reports/Medical Records***		***EMR Integration***		***Data Display & Dissemination***
	Chair: Peter Tarczy-Hornoch		Chairs: Erwin Bottinger and Justin Starren		Chairs: Tara Matise
	Mission: Inventory and coordinate standards for storing sequence/variant data; discuss approaches to the implementation of clinical decision support tools in electronic medical records.		Mission: Develop consensus and concepts for EMR integration of genomic information and the delivery of clinical genomic decision support utilizing EMR. Delineate common and distinct approaches and challenges for EMR integration of relevant genomic information for clinical pharmacogenomic, monogenic disorders, and common disease risk applications.		Mission: This group is charged with creating data browsers to display statistical results from PAGE and to interact with dbGaP and other collaborators in matters related to PAGE data display.
	NHGRI Staff: Lucia Hindorff		NHGRI Staff: Rongling Li		NHGRI Staff: Lucia Hindorff

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Other Working Groups		***Instruments and Measures***	***Pharmacogenomics (eMERGE-PGx)***	***Cancer***	***SNP Selection & Quality Control***
		Chair: Amy McGuire and Gail Henderson	Chair: Dan Roden	Chairs: Charis Eng and Gail Jarvik	Chairs: Chairs: Chris Haiman and Chris Carlson Mission: This group is charged with developing
		Mission: Coordinate development of instruments to measure psychosocial outcomes related to returning results.	Mission: The project group plans to sequence patients on a platform that covers 84 "VIP" pharmacogenes. Then they will develop a validation pipeline and figure out how to display these variants in the EMR and create decision support for them.	Mission: Improve implementation of recommendations for IHC/MSI and genetic screening for various forms of cancer and create a resource to evaluate successful implementation of screening. Integrate germline and tumor sequencing with treatment and outcomes including family pairs in order to understand variable penetrance, expressivity, and clinical outcomes. Link to family history and TCGA project.	Mission: This group is charged with developing targeted SNP lists for PAGE and coordinating genotyping quality control procedures. They also led the planning of the Metabochip pilot and restructuring of PAGE genotyping from targeted variants to Metabochip genotyping.
		NHGRI Staff: Nicole Lockhart	NHGRI Staff: Rongling Li, Simona Volpi	NHGRI Staff: Teri Manolio	NHGRI Staff: Lucia Hindorff
		Pediatrics Working Group		***Family History***	***Ethnicity & Ancestry***
		Chair: Ellen Clayton		Chairs: Geoff Ginsburg and Lori Orlando	Chairs: Dan Stram
		Mission: Explore and attempt to develop standardized approaches to addrsesing the unique ethical, legal, and practical challenges relating to returning results in studies involving pediatric populations.		Mission: Increase accuracy of FH information through validation and develop a 'user interface' for patients and providers for FH. Implement science to integrate FH into the clinical workflow. Work towards integration of all data and development of disease risk models. Assemble a group to facilitate incorporation of FH initiatives into large cohort studies.	Mission: This group was initially charged with developing a policy to deal with admixture in PAGE, a very ethnically diverse study. Most studies now have GWAS, AIMs or Metabochip data and are using principal components analysis, so working group is only meeting when needed.
		NHGRI Staff: Jean McEwen		NHGRI Staff: Teri Manolio	NHGRI Staff: Lucia Hindorff
				Pharmacogenomics	***Metabochip Pilot***
				Chairs: Alan Shuldiner, Howard McLeod, and Mark Ratain	Chairs: Kari North
				Mission: Identify one or more collaborative demonstration projects that would advance implementation of pharmacogenomics into clinical practice.	Mission: Mission: This working group is an "umbrella group" for the individual PAGE Metabochip analysis groups to coordinate and discuss common approaches. Midway through PAGE, they proposed and implemented a plan for a pilot study of 5000 African Americans; upon successful completion of the pilot, they are now overseeing the expansion of Metabochip genotyping to ~70,000 non-European participants.
				NHGRI Staff: Teri Manolio	NHGRI Staff: Lucia Hindorff
				Periodontal Microbiome	***Statistical Analysis***
				Chair: Murray Brilliant	Chairs: Charles Kooperberg and Marylyn Ritchie
				Mission: Implement Warfarin pharmacogenetics testing prior to dental procedures. Gain a better understanding of the risks for T2D (including onset, severity, and control), the genetics of T2D, and the role of environment in T2D.	Mission: Review and ensure consistency of statistical approaches across PAGE manuscripts. Most working groups have now settled on a consistent approach, so group is only meeting when needed.
				NHGRI Staff: Teri Manolio	NHGRI Staff: Lucia Hindorff
				Clinical/Research Interface	***PheWAS***
				Chairs: Marc Williams and Pearl O'Rourke	Chairs: Marylyn Ritchie and Sarah Pendergrass
				Mission: To better understand real and perceived barriers as well as appropriate and inappropriate concerns to movement from research into the clinical realm. The group will catalog and review current and planned initiatives and propose collaboration with existing initatives as well as new reseach to address the gaps and to facilitate responsible migration of genetic information into clinical implementation.	Mission: Develop and implement plans to utilize breadth of PAGE phenotype data using Phenome-wide Association Study (PheWAS) and other approaches; interact with other related consortia.
				NHGRI Staff: Teri Manolio	NHGRI Staff: Lucia Hindorff

Other Programs Involving Related Activities

Mendelian Seq. Centers

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Clin Action Database